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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,672	04/18/2002	Joelle Thonnard	BM45395	1681

25308 7590 08/16/2004

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,672	THONNARD, JOELLE	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-50* is/are pending in the application.

4a) Of the above claim(s) *29,31,32,34,37,38,40-43,46 and 48-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,30,33,35,36,39,44,45 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/13/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment

1. Applicant's response filed on 5/28/04 is acknowledged.

Election/Restriction

2. Applicant's election of Group I, claims 28, 30, 33, 35, 36, 39 and 44-45 drawn to polypeptide, SEQ ID NO: 2 is acknowledged. Since no arguments have been put forth in response to restriction, the election is considered without traverse.

Status of claims

3. Claims 28-50 are pending.

Claims 28, 30, 33, 35, 36, 39 and 44-45 have been elected for prosecution in this application. However, the examiner has included Group IV invention, claim 47 (see previous office action on restriction) drawn to a method for inducing an immune response using a polypeptide as it is drawn to the first method of use under 35 U.S.C. 121 and 372. Therefore Claims 28, 30, 33, 35, 36, 39, 44-45 and 47 are under examination.

Claims 29, 31, 32, 34, 37, 38, 40-43, 46, 48 and 49 and 50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group of inventions and there being no allowable generic or linking claim.

Priority

4. This application is a 371 OF PCT/EP 00/05852, 6/23/2000, which claims priority under 35, U.S.C. 119 (a)- (d) to U.K 9914945031.2, 6/25/1999 is acknowledged. However, a copy of certified priority document U.K 9914945031.2, 6/25/1999 is not present in the application. Applicant is advised to submit the same for completion of the present application filed under 35 U.S.C. 121 and 372.

Information Disclosure Statement

5. The Information Disclosure Statement filed on 12/13/01 is acknowledged and a signed copy of the same is enclosed to this office action.

Specification Informalities/Claim objections

6. This application is informal in the arrangement of the specification. Applicant attention is directed to MPEP 608.01(a). For example: Claims shoud begin with "I claim" or "'We claim" or "What is claimed is".

Applicant's attention is also directed to 37 CFR 1.74 See MPEP § 608.01(f) in reference to brief description of the drawing(s).

It is noted recitation of "□ g " on page 38, lines 17-18, page 39, line 23. It is not clear what is it stands for? If it is milligram, it should be recited as "mg " or if it is microgram, it should be "μg". Appropriate correction is required through out the specification.

Recitation of XL Fit software program, on page 58 is noted. However, the software programs can be readily changed with rapidly changing technology and therefore, may not be available to the public. Therefore, applicant is advised to amend the specification and use some other means to recite the program. Appropriate correction is required.

Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim objections

Claim 39 is objected to because of the following informalities: Please note claim 39 depends on canceled claim 22. Appropriate correction is required.

In order to advance the prosecution, the examiner is reading the limitations of claim 28 into claim 39.

It appears that there is a typographical error or oversight in writing the claim 28. As written it appears that the isolated polypeptide when administered induces an antibody or T cell immune response to "a" polypeptide having the sequence of SEQ.ID.NO: 2. However, it should read as "the" polypeptide having the sequence SEQ.ID.NO: 2 because subject is administered with the isolated polypeptide.

Claim 47 is drawn to a method for inducing an immune response in a mammal comprising administration of polypeptide of claim 28. In order to complete the claim, the claims should read as a method for inducing an immune response in a mammal comprising administration of the polypeptide of claim 28 to said mammal?

Claim Rejections - 35 USC 112

7 The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying.

8. Claims 28, 33, 35, 39, 44, 45 and 47 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published at www.uspto.gov (O.G. published January 30, 2001). This is a written description rejection.

The claims are drawn to an isolated polypeptide comprising a member selected from the group consisting of an amino acid sequence matching SEQ.ID.NO: 2 and an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids or 20 amino acids that matches an aligned contiguous segment of SEQ.ID.NO: 2. Claims are also drawn to fusion protein comprising said peptide/fragments and a vaccine composition comprising said peptide/ fragments and a method of inducing immune response using said peptide/fragments.

Please note: The examiner is viewing claims 28 (a) and 30 as an isolated polypeptide comprising the amino acid sequence as set forth in SEQ.ID.NO: 2 or an isolated polypeptide comprising the amino acid sequence matching SEQ.ID.NO: 2 because an isolated polypeptide comprising an amino acid "matching" in 28(a) is treated as a closed language and is interpreted as an isolated polypeptide comprising the amino acid sequence matching SEQ.ID.NO: 2 because the Webster's English dictionary defines "match" as exactly alike.

The specification describes as part of the invention, an isolated polypeptide comprising the amino acid sequence, SEQ ID NO: 2, which is encoded by BASB111 gene from *M.catarrhalis* strain Mc 2931, ATCC 43617. The specification also teaches that this full-length protein contains 276 amino acids and is useful in diagnosing *M.catarrhalis* infection. However, the immunological function of this gene or its product in assessing Otitis media has not yet been identified. Further, the specification does not an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids or 20 amino acids or vaccine comprising said fragments (i.e., 15 amino acids or 20 amino acids) or fusion protein comprising said fragments (i.e., 15 amino acids or 20 amino acids). Therefore, said fragments do not meet the guidelines on written description.

The specification fails to disclose any substitution, insertion or deletion or change in a polypeptide SEQ.ID.NO: 2 to obtain an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids or 20 amino acids. The specification does not describe any use of said fragments as claimed (comprising, open language) in identifying *M.catarrhalis*

infection (Ottis media). None of the above fragments meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, the specification fails to teach the claimed fragments and do not satisfy the written description guidelines because an isolated immunogenic polypeptide comprising (open language) at least 15 amino acids plus unlimited and unknown amino acids and an isolated polypeptide comprising 20 amino acids 2 plus unlimited and unknown amino acids would result in an unknown fragments without any structure and other identifying characteristics such as function. Thus, fragments as claimed are broader than SEQ.ID.NO: 2. Further, inducing an immune response is not an identifying characteristic (function) of a fragment because there are many fragments with the same function in a polypeptide and such variants are not distinguishable from each other. Thus variants as claimed are uncharacterized by this specification and are not asserted to belong to any known family of proteins such as outer membrane proteins of *M.catarrhalis.* The specification fails to teach the structure or relevant identifying characteristics sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived.

See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

9. Claims 28, 33, 35, 39, 44, 45 and 47 are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO: 2, fusion protein comprising the amino acid sequence SEQ ID NO: 2 and an immunogenic composition comprising said polypeptide SEQ ID NO: 2 does not reasonably provide enablement for an immunogenic polypeptide comprising a fragment of at least 15 or 20 amino acids that matches an aligned contiguous segment of SEQ.ID.NO: 2., fusion protein comprising said fragments or a vaccine composition comprising an isolated polypeptide comprising an amino acid sequence SEQ.ID.NO: 2 or fragments of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims have been discussed supra as above in Paragraph # 8.

The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is drawn to recombinant isolated polypeptide comprising the amino acid sequence, SEQ ID NO: 2, which is encoded by BASB111 gene from *M.catarrhalis* strain Mc 2931, ATCC 43617. The specification also teaches that the full-length

polypeptide, SEQ.ID.NO: 2 contains 276 amino acids and is useful in diagnosing *M.catarrhalis* infection. Further, the invention teaches that the polypeptide, SEQ.ID.NO: 2 could be used as an immunogen in formulating immunogenic composition in Freund's adjuvant to immunize mice for raising anti polypeptide, SEQ.ID.NO: 2 antibodies.

The state of the art prior art is devoid of making or using fragments such as an isolated immunogenic polypeptide comprising (open language) at least 15 amino acids plus unlimited and unknown amino acids and an isolated immunogenic polypeptide comprising 20 amino acids 2 plus unlimited and unknown amino acids as claimed broadly in bacterial infections especially in *M.catarrhalis* infections.

The predictability of making and using fragments of a polypeptide in generating antibodies, sufficient to specifically diagnose otitis media and respiratory disease caused by Moraxella catarrhalis infections or sufficient to elicit a protective immune response against otitis media and respiratory disease caused by Moraxella catarrhalis infection is acknowledged to be unpredictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid sequences (i.e. fragments) for different aspects of biological activity cannot be predicted a priori and must be determined empirically on a case-by-case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while

replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Thus, it is apparent that change in a peptide leads to loss of binding property of that peptide.

The specification provides no working examples demonstrating (i.e., guidance) enablement for an immunogenic fragment comprising (open language) at least 15 amino acids or 20 amino acids plus unlimited amino acids, fusion protein comprising said fragments, immunogenic composition comprising said fragments of SEQ ID NO: 2 or a method of diagnosing *M.catarrhalis.* infection using said broadly claimed fragments. Furthermore, it is unclear whether an immunogenic polypeptide comprising at least 15 amino acids or 20 amino acids, fusion protein comprising said fragments of *M.catarrhalis.* can be used for identifying *M.catarrhalis.* infection. Thus, fragments comprising at least 15 or 20 amino acids must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis.

The specification fails to provide an enabling disclosure for using fragments of SEQ.ID.NO: 2 because it fails to provide guidance how a fragment of SEQ.ID.NO: 2 is useful in diagnosing *M.catarrhalis* infections or for screening anti-microbial drugs. The specification

provides no disclosure how a fragment of SEQ.ID.NO: 2 may be used as a target for a *M.catarrhalis* infection because it fails to provide guidance whether this variant has the ability to bind to anti- *M.catarrhalis.* antibodies. Therefore, the skilled artisan would not be able to use such broadly claimed fragments. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as broadly claimed.

Since, the specification lacks a written description for fragments of SEQ ID NO: 2 as claimed and the specification fails to provide an enabling disclosure other than polypeptide SEQ.ID.NO: 2 as the specification does not teach and provide any guidance how to make an immunogenic polypeptide comprising a fragment of at least 15 or 20 amino acids that matches an aligned contiguous segment of SEQ.ID.NO: 2, it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed structure of the claimed polypeptide fragments of SEQ ID NO: 2 and their use in identifying specific *M.catarrhalis* infections. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

10. Claims 44-45 and claim 28 (as a vaccine composition only) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims are drawn to a vaccine composition comprising an isolated polypeptide comprising a member selected from the group consisting of an amino acid sequence matching SEQ.ID.NO: 2 and an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids or 20 amino acids and at least one other *M.catarrhalis* antigen in a pharmaceutically acceptable carrier.

Instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The definition of "vaccine" is broad, it is not so broad to cover **any** use of a substance on or in the body of a subject, only those uses intended to prevent, treat, or cure a disease within the animal to which the substance was administered.

Enablement of a "vaccine composition" is considered to rest on a teaching of in vivo administration for purposes consistent with the intended use disclosed in the specification. The disclosed intended use for the claimed vaccine is for the treatment of otitis media and respiratory disease caused by Moraxella catarrhalis infections. Thus, the nature of the invention is a therapeutic composition used in the treatment or prevention. In the instant application, the animal to which the claimed composition is administered is merely being used as a bioreactor to make the antibodies (example 5) that will ultimately be used *in vitro*. In addition, the instant specification does not teach how to use the composition, without undue experimentation, for the prevention, treatment, or cure of a disease in the animal to which the substance is administered.

The specification discloses the claimed composition as a vaccine can be used in mice model (example 3). There is insufficient guidance which would enable one skilled in the art to use the claimed compositions for their intended purpose, viz., for the generation of a protective immune response against otitis media and respiratory disease caused by Moraxella catarrhalis infections. At the time the invention was made, vaccines comprising the claimed polypeptide/fragments were not routinely used for the treatment of otitis media and respiratory diseases. The specification lacks guidance by way of general methods or working examples which teach an "effective amount" of the vaccine which would be used for this purpose. Lack of

working examples is given added weight in cases involving an unpredictable and undeveloped art, such as immunotherapy of otitis media and respiratory diseases. It is unpredictable whether the claimed composition, which is disclosed as being only immunogenic, would have the added property of generating the protective immune response sufficient to inhibit the otitis media and respiratory diseases because the prior art discloses that vaccine development is at the antigen identification stage and testing of these protective antigens is by testing them in animal models or clinical testing of these antigens (see review article by McMichael, 2000, Microbes and Infection 2; 561-568) The specification has not disclosed a link or nexus between generating protective immunity using the claimed polypeptide/fragments and preventing or curing *M.catarrhalis* infections or Ottis media. Further, it is not common in the art of immunotherapy to use the claimed compositions for this purpose. Accordingly, there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed composition/vaccine effective for its intended use. Therefore, undue experimentation would be required to make and use the invention.

It is acknowledged that weight is given to every term in claims 44-45. This is why the instant claims drawn to vaccines are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same composition and formulations thereof as claimed.

Claim Rejections - 35 USC 112, second paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claim 45 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 is vague in reciting "at least one other M.catarrhalis antigen", as claim 44 does not refer to M.catarrhalis antigen.

Claim Rejections - 35 USC 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The transitional limitation "comprises" similar to the limitations, such as, "has", "includes," "contains," or "characterized by," represents open-ended claim language and therefore does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-1]. See *Molecular Research Corp. v. CBS, Inc., 793 F2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App.1948)* ("comprising" leaves "the claim open. for the inclusion of unspecified ingredients even in major amounts". On the other hand, the limitation "consisting of represents closed claim language and excludes any element, step, or ingredient not specified in the claim. In *re Gray, 53 F. 2d 520, Il USPQ 255 (CCPA 1931); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948).*

14. Claims 28, 30, 33, 35, 44 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Christensen et al Clin Diagn Lab Immunol. 1996 Nov; 3(6): 717-21.

Claims are directed to an isolated polypeptide comprising a member selected from the group consisting of (a) an amino acid sequence that matches SEQ.ID.NO: 2 (b) an immunogenic fragment comprising at least 15 amino acids or 20 amino acids that matches an aligned contiguous segment of SEQ.ID.NO: 2 when administered with a carrier induces an antibody response or T-cell response. Claims are also directed to a vaccine composition comprising said polypeptide/fragments.

Christensen et al disclose isolated polypeptides by SDS-PAGE from outer membrane proteins i.e., OMP from different strains, in a buffer (pharmaceutical carrier) from M.catarrhalis (see materials and methods).

The OMP patterns obtained by SDS-PAGE of the seven *M. catarrhalis* strains were shown in Fig. 1. Approximately 25 bands with molecular masses of between 140 and 16 kDa could be identified, with six to eight of these being the major bands A to H, with molecular masses of 98, 84, 72, 69, 56, 43, 28, and 21 kDa recognized for individual strains.

The lower-molecular-weight OMP 28 kD (figure 1, see in the next page) polypeptide appears to be same as the claimed polypeptide, SEQ.ID.NO: 2 having 276 amino acids because molecular weight of an amino acid is approximately 110 daltons. Therefore, 28 kD protein read on claims. The disclosed OMP preparations read on immunogenic composition as outer membrane proteins bind to the convalescent sera (see figure2). Thus, the prior art anticipated claims 28, 30, 33 and 35. The same OMP preparation reads on a vaccine composition because vaccine is treated as intended use of said composition recited in claims 44 and 45. As OMP contains several antigens in the preparation, it meets the limitation "one other Moraxella antigen" of claim 45.

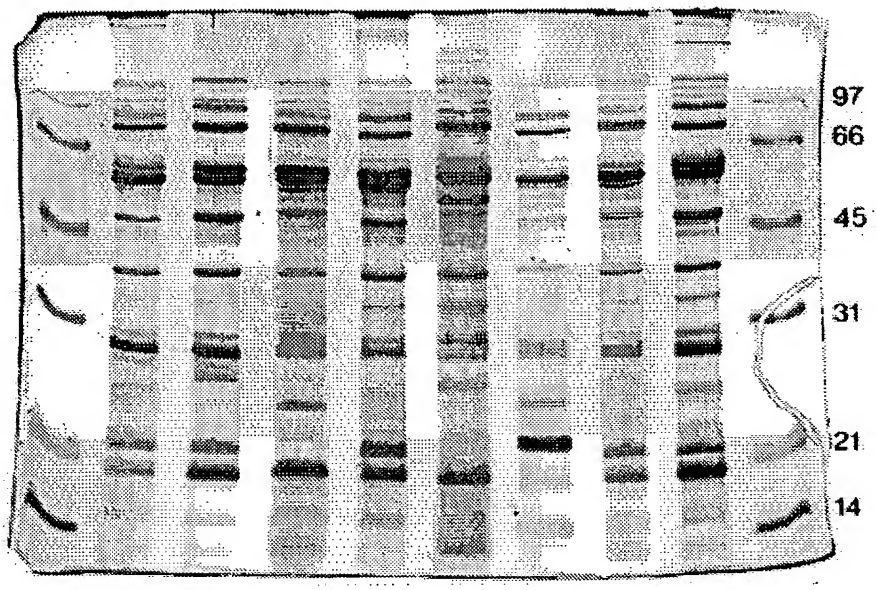


FIG. 1. Coomassie blue-stained SDS-polyacrylamide gels of OMP preparations from strains of *M. catarrhalis*. The outside lanes contain molecular mass markers. Molecular masses (in kilodaltons) are given on the right. Lane 1, type strain; lanes 2 and 3, respiratory tract isolates from Sweden and Denmark, respectively; lanes 4 and 5, blood culture isolates from the United States and Denmark, respectively; lane 6, eye isolate from the United States; lane 7, mixture of OMPs from six strains of *M. catarrhalis* (lanes 1 to 6); lane 8, strain F 48 (see Materials and Methods).

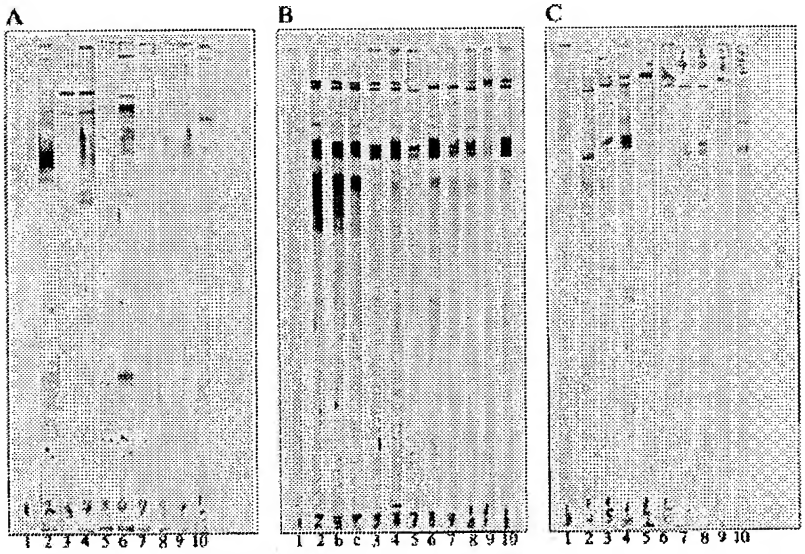


FIG. 2. Results of Western blot analysis examinations in which OMPs of *M. catarrhalis* were tested with sera from four patients suspected of having bronchopulmonary infection caused by *M. catarrhalis*. Sera were tested for the presence of IgM (A), IgG (B), and IgA (C) against OMPs of *M. catarrhalis*. Lanes 1 and 2, negative and positive controls, respectively (i.e., no addition of serum and addition of serum from a patient whose blood yielded growth of *M. catarrhalis* on culture); lanes 2b and 2c, the positive control was diluted 1:2 and 1:4, respectively; lanes 3 and 4 (sera from patient 1), 5 and 6 (sera from patient 2), 7 and 8 (sera from patient 3), and 9 and 10 (sera from patient 4) provide results for acutes- and convalescent-phase sera (for each pair of lanes, respectively) from four patients with different antibody response patterns; IgM-class antibody responses are seen for patients 1, 2, and 4; increased IgG-class antibody responses in convalescent-phase sera are seen for all patients; increased IgA-class antibody responses in convalescent-phase sera are seen for patients 1, 2, and 4.

Applicant's use of the open-ended term "comprising " in the claim 28 fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Therefore, the claims read on the disclosed isolated polypeptide, fragments and a vaccine composition (intended use) because OMPs from *M.catarrhalis* contains many proteins.

Outer membrane 28kD protein from M.catarrhalis inherently contains an isolated polypeptide comprising SEQ.ID.NO: 2 as it contains all proteins produced by this organism. Characteristics such as SEQ.ID.NO: 2 are considered as inherent properties of the 28kD polypeptide that was present in the OMP disclosed by the prior art. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). Since the Office does not have the facilities for examining and comparing applicants' claimed isolated polypeptide comprising SEQ.ID.NO: 2 with the polypeptide of prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

15. Claims 28, 33 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Murphy et al 1993, Database: PIR_78, Acession number JN0751.

Claims are discussed supra.

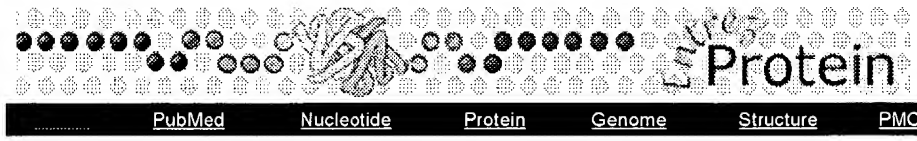
Murphy et al in Acession number JN0751disclose an isolated polypeptide comprising an immunogenic polypeptide comprising a fragment of at least 15 amino acids or 20 amino acids that matches 100% with an aligned contiguous segment of SEQ.ID.NO: 2 (please see the

sequence alignment, 3rd line from position 140-173, QY represents SEQ.ID.NO: 2 of the claimed invention and Db represents the prior art protein)

```
JN0751
Outer membrane 30K protein - Pasteurella haemolytica
N;Alternate names: ORF1
C;Species: Pasteurella haemolytica
C;Date: 14-Jul-1994 #sequence_revision 14-Jul-1994 #text_change 20-Aug-1999
C;Accession: JN0751
R;Murphy, G.L.; Whitworth, L.C.
Gene 129, 107-111, 1993
A;Title: Analysis of tandem, multiple genes encoding 30-kDa membrane proteins
in Pasteurella haemolytica A1.
A;Reference number: JN0751; MUID:93328110; PMID:8335249
A;Accession: JN0751
A;Molecule type: DNA
A; Residues: 1-277 <MUR>
Across-references: GB: L11037; NID: g349529; PIDN: AAA25538.1; PID: g349530
A; Experimental source: serotype A1
A;Note: this protein displays a high degree of identity with an Escherichia
coli inner membrane lipoprotein and an haemophilus influenzae membrane
protein
C;Comment: This protein is important in eliciting immunity to pneumonic
pasteurellosis.
C;Superfamily: lipoprotein-28
C;Keywords: membrane protein

  Query Match             12.3%;  Score 34;  DB 2;  Length 277;
  Best Local Similarity   100.0%;  Pred. No. 8e-26;
  Matches   34;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps 0;

Qy        140 IAVPNDPSNLARALILLEKQGLIKLKDNTNLFST 173
              |||||||||||||||||||||||||||||||||
Db        141 IAVPNDPSNLARALILLEKQGLIKLKDNTNLFST 174
```



JN0751. Outer membrane 30...[gi:541237]

LOCUS JN0751 277 aa linear BCT 20-AUG-1999
DEFINITION Outer membrane 30K protein - Pasteurella haemolytica.
ACCESSION JN0751
VERSION JN0751 GI:541237
DBSOURCE pir: locus JN0751;
summary: #length 277 #molecular-weight 29992 #checksum 3218
; superfamily: lipoprote ;
PIR dates: 14-Jul-1994 #sequence_revision 14-Jul-1994 #text_change
20-Aug-1999 .
KEYWORDS membrane protein.
SOURCE Mannheimia haemolytica
ORGANISM Mannheimia haemolytica
Bacteria; Proteobacteria; Gammaproteobacteria; Pasteurellales;
Pasteurellaceae; Mannheimia.
REFERENCE 1 (residues 1 to 277)
AUTHORS Murphy,G.L. and Whitworth,L.C.
TITLE Analysis of tandem, multiple genes encoding 30-kDa membrane
proteins in Pasteurella haemolytica A1
JOURNAL Gene 129 (1), 107-111 (1993)
MEDLINE 93328110
PUBMED 8335249
COMMENT This protein is important in eliciting immunity to pneumonic
pasteurellosis.
FEATURES Location/Qualifiers
source 1..277
/organism="Mannheimia haemolytica"
/db_xref="taxon:75985"
Protein 1..277
/product="Outer membrane 30K protein"
/note="ORF1"
ORIGIN
1 msfkkilgva lvsalaltac keekkaesta apaaqapaki kvgvmsgpeh tvaeraaqia
61 kekyglevef vlfndyalpn tavskgdlda nafqhkpyld kdsqskglnn lvivgntfvy
121 plagyskkvk nvselaegav iavpndpsnl aralillekq gliklkdntn lfstsvdiie

181 npknlkikev dtsiaakald dvdlavvnnt yagqvglntq dhgvfveskd spyvniivar
241 qdnkdaanvq nfiksyqtee vyqeaqkhfk dgvvkgw

and thus anticipated claims 28, 33 and 35. The prior art polypeptide reads on claims because the disclosed immunogenic fragment comprises more than 20 amino acids and is common in the art of immunology to use a peptide with five amino acids to induce an antibody response in animals, therefore, the disclosed polypeptide comprising 276 amino acids is inherently immunogenic and thus comprises an immunogenic fragments as claimed in claims. Therefore, the claimed invention is anticipated by the prior art.

15. Claims 28, 33, 35, 39, 44, 45 and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Breton U.S.Patent 6673910.

Claims have been discussed supra.

Breton discloses an isolated polypeptide comprising an amino acid sequence SEQ.ID.NO: 2991 which has 118 amino acids and is 100% identical with an aligned contiguous segment of SEQ.ID.NO: 2 from position 47-103 (please see the sequence alignment, QY indicates SEQ.ID.NO: 2 of the claimed invention and Db represents the prior art protein)

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US-09-540-236-2991
; Sequence 2991, Application US/09540236
; Patent No. 6673910
; GENERAL INFORMATION:
;  APPLICANT: Gary L. Breton et al.
;  TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO
MORAXELLA CATARRHALIS
;  TITLE OF INVENTION: FOR DIAGNOSTICS AND THERAPEUTICS
;  FILE REFERENCE: 2709.2005-001
;  CURRENT APPLICATION NUMBER: US/09/540,236
;  CURRENT FILING DATE: 2000-04-04
;  NUMBER OF SEQ ID NOS: 3840
; SEQ ID NO 2991
;   LENGTH: 118
;   TYPE: PRT
;   ORGANISM: M.catarrhalis
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US-09-540-236-2991

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  Query Match             20.7%;  Score 57;  DB 4;  Length 118;
  Best Local Similarity   100.0%;  Pred. No. 2.2e-47;
  Matches   57;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps0;

Qy          47 PEQAVAEVAGQVAKEKYNLTVELVEFNDYAMPNSAVSKGELDANAMQHKPYLEKDSQ 103
               |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          57 PEQAVAEVAGQVAKEKYNLTVELVEFNDYAMPNSAVSKGELDANAMQHKPYLEKDSQ 113
```

and thus anticipated claims 28, 33 and 35. The prior art discloses maltose receptor (outer membrane protein of E.coli) as a peptide fusion partner (column 34, lines 15-30 in patent) and thus discloses fusion protein as claimed in claim 39. Further the prior art discloses a vaccine composition (intended use of composition) comprising M.catarrhalis polypeptide, SEQ.ID.NO: 2991 with pharmaceutical carrier such as buffer, adjuvant, glycerol etc (see column 37-38) or killed E.coli preparation with an immunogenic fragment of peptide of the invention expressed on its surface or E.coli lysate, wherein the killed E.coli acts a carrier (see column 39, lines 58-63). Further, the prior art discloses one or more surface proteins as vaccine composition (see column 37, lines 8-20) for *M.catarrahalis* and thus anticipates a vaccine composition comprising immunogenic fragments /polypeptide and one other *M.catarrhalis* antigen in a pharmaceutical carrier as claimed in claims 44-45. The prior art also anticipated claim 47, a method for inducing an antibody response as mice or rabbit or hamsters can be immunized (administered) with immunogenic fragment such as the disclosed polypeptide, SEQ.ID.NO: 2991(see column 40, lines 16-21). Therefore, the claimed invention is anticipated by the prior art.

17. Claims 30 and 36 are free of prior art.

Claims 30 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Remarks

Remarks

18. No claims are allowed

Conclusion

19. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

20. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Respectfully,

Padma Baskar 8/6/04

Padma Baskar Ph.D.